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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,948	02/17/2004	Mark D. Erion	MET-016XDT	2285

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EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
02/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/780,948	ERION ET AL.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *147 and 151* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05222008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 95-97,120,121,124-132,147,151,168-241,245,251-290,293,299-338,341,347-386,389 and 395-397.

Continuation of Disposition of Claims: Claims rejected are 95-97,120,121,124-132,168-241,245,251-290,293,299-338,341,347-386,389 and 395-397.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Compound H and troglitazone (species election) in the reply filed on June 18, 2007 is acknowledged.

Applicant's Response Dated October 9, 2008

2. Claims 95-97, 120-121, 124-132, 147, 151, 168-241, 245, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 are pending. An action on the merits of claims 95-97, 120-121, 124-132, 147, 151, 168-241, 245, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 is contained herein below.

3. The rejection of claims 95-97, 120-121, 124-132, 168-241, 245, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record set forth in the Office Action dated May 9, 2008.

4. The objection to claims 147 and 151 is maintained for the reasons of record set forth in the Office Action dated May 9, 2008.

Rejections of Record Set Forth in the Office Action Dated May 9, 2008

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 95-97, 120-121, 124-132, 168-241, 245, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a mammal having diabetes comprising the administration of a pharmaceutically effective amount of an

insulin sensitizer agent and a pharmaceutically effective amount of an FBPase inhibitor or prodrug or salt thereof, wherein said insulin sensitizer agent is troglitazone or rosiglitazone and wherein said FBPase inhibitor is Compound A, B, C, D, E, F, G, H, I, J or K, does not reasonably provide enablement for treating a mammal having diabetes comprising the administration of a pharmaceutically effective with any compound of formula I or IA in combination with any insulin sensitizer agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

1. the breadth of the claims;
2. the nature of the invention;
3. the state of the prior art;
4. the level of one of ordinary skill in the art;
5. the level of predictability in the art;
6. the amount of direction provided by the inventor;
7. the existence of working examples; and
8. the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 95-97, 120-121, 124-132, 168-241, 245, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 are drawn to method of treating a mammal having diabetes comprising the administration of a pharmaceutically effective amount of an insulin sensitizer agent and a pharmaceutically effective amount of an FBPase inhibitor or prodrug or salt thereof.

Undue experimentation is required to determine which compounds would be useful as an insulin sensitizer agent and/or FBPase inhibitor for which the instant invention is applicable and to determine which of these combinations would be useful in treating diabetes in a mammal. There has not been provided adequate guidance in the written description for accomplishing such, as only Compounds A-K (FBPase inhibitor) in combination with troglitazone or rosiglitazone (insulin sensitizer agent) were assessed, out of the numerous insulin sensitizer agents known in the art, not to mention the near infinite number of compounds and classes of compounds embraced by the instantly claimed formulae I and IA. While it is noted that an assay has been described for identifying other FBPase inhibitors, without guidance as to what molecules would likely effect FBPase activity, undue trial and error experimentation would be required to screen through the myriad of different chemical molecules embraced by formulae I and IA to determine those with the desired FBPase inhibiting activity and that would function in the claimed method of treating diabetes. There is nothing inherently wrong with defining some part of an invention in functional terms; however, a functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is

used. Functional descriptions of chemical compounds/compositions must be coupled with a known or disclosed correlation between function and structure. It is also noted that there is a great deal of unpredictability in the art.

The compounds of formulae I and IA do not share a common, substantial chemical core. Further, Compounds A-K do not share a common, substantial chemical core. There is no discernable pattern as to which compounds of formula I or IA would inhibit FBPase activity. The art at the time the invention was made fails to establish predictability with regard to the properties of the FBPase inhibitors and insulin sensitizer agents needed to perform the methods as instantly claimed. It is noted that while there are some working examples using certain compounds of formula I or IA (Compounds A-K) in combination with troglitazone or rosiglitazone, it is not seen as sufficient to support the breath of the claims. The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to enable the use of any other compounds of formula I or IA or other insulin sensitizer agents. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves. See *In re Gardner* et al. 166 USPQ 138 (CCPA 1970).

7. Applicant's arguments filed October 9, 2008 have been fully considered but they are not persuasive. Applicant argues that a considerable amount of experimentation is permissible, if it is merely routine. Applicant argues that 1) an assay has been described for identifying other FBPase inhibitors; 2) the specification teaches those

insulin sensitizers suitable for use in the claimed methods; and 3) those skilled in the art would have had adequate knowledge as to the compounds suitable for use as FBPase inhibitors.

Applicant's arguments have been fully considered; however, the examiner respectfully disagrees. As set forth supra, the Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves. Contrary to applicant's assertion, the specification does not teach those insulin sensitizers suitable for use in the claimed methods but rather set forth a laundry list of non-limiting examples. Page 127 of the specification states, "While such disclosures constitute a large number of insulin sensitizers, the instant invention is not so limited and can utilize any insulin sensitizer compound." In regards to applicant's contention that the skilled artisan would be able to predict which compounds of Formulae I and IA are suitable for use in the claimed methods, no guidance or rationale has been set forth which would lead the skilled artisan to make such predictions. As set forth supra, compounds of formulae I and IA do not share a common, substantial chemical core. Further, Compounds A-K do not share a common, substantial chemical core. There is no discernable pattern as to which compounds of formula I or IA would inhibit FBPase activity. The art at the time the invention was made fails to establish predictability with regard to the properties of the FBPase inhibitors and insulin sensitizer agents needed to perform the methods as instantly claimed. Applicant's attention is directed to Belikov (Pharmaceutical Chemistry (1993), Vol. 1, pages 43-47). Belikov teaches, "Finding the relationship between the

chemical structure and action of substances on an organism is of tremendous importance in a broad biological aspect. Solving this problem would make it possible to realize purposeful synthesis of medicaments having prescribed pharmacological action. An idea of the presence of connection between the structure of organic compounds and their biological activity was advanced for the first time as early as in 1869. However, despite more than centuries of efforts made by many generations of scientists, so far only certain regularities have been found."

Conclusion

8. Claims 95-97, 120-121, 124-132, 147, 151, 168-241, 245, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 are pending. Claims 95-97, 120-121, 124-132, 168-241, 245, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 are rejected. Claims 147 and 151 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. No claims are allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Patrick T. Lewis/
Primary Examiner, Art Unit 1623

/PL/